CLAIMS

1. A tyrosine kinase inhibitor protein consisting of the cap region of a c-Abl protein or a functional equivalent thereof.
2. A tyrosine kinase inhibitor protein according to claim 1 wherein the c-Abl protein is a mammalian c-Abl protein.
3. A tyrosine kinase inhibitor protein according to claim 2 wherein the c-Abl protein is human.
4. A tyrosine kinase inhibitor protein according to claim 3 wherein the c-Abl protein is type 1a c-Abl.
5. A tyrosine kinase inhibitor protein according to claim 3 wherein the c-Abl protein is type 1b c-Abl.
6. A tyrosine kinase inhibitor protein according to claim 4 consisting of amino acids 1-61 of type 1a c-Abl.
7. A tyrosine kinase inhibitor protein according to claim 5 consisting of amino acids 1-80 of Type 1b c-Abl.
8. A tyrosine kinase inhibitor protein according to claim 2 wherein the c-Abl protein is murine.
9. A tyrosine kinase inhibitor protein according to claim 8 wherein the c-Abl protein is type I c-Abl.
10. A tyrosine kinase inhibitor protein according to claim 8 wherein the c-Abl protein is type IV c-Abl.
11. A tyrosine kinase inhibitor protein according to claim 9 consisting of amino acids 1-63 of type I c-Abl.
12. A tyrosine kinase inhibitor protein according to claim 10 consisting of amino acids 1-80 of type IV c-Abl.
13. A tyrosine kinase inhibitor protein or functional equivalent thereof according to any one of claims 1-12 which inhibits a tyrosine kinase protein containing SH2 and SH3 domains.
14. A tyrosine kinase inhibitor protein or functional equivalent according to claim 13 which inhibits Abl, Src or Fyn.
15. A tyrosine kinase inhibitor protein or functional equivalent thereof according to claim 13 which inhibits an oncogenic form of said tyrosine kinase protein containing SH2 and SH3 domains.

16. A tyrosine kinase inhibitor protein or functional equivalent thereof according to claim 15 which inhibits an oncogenic form of Abl, Src or Fyn.

17. A tyrosine kinase inhibitor protein or functional equivalent thereof according to claim 16 which inhibits an oncogenic form of Abl.

18. A tyrosine kinase inhibitor protein or functional equivalent thereof according to claim 17 which inhibits BCR-Abl.

19. A fusion protein comprising a tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1 to 18 fused to a marker domain.

20. A fusion protein according to claim 19 wherein the marker domain is green fluorescent protein.

21. An antibody that binds to a tyrosine kinase inhibitor protein or functional equivalent according to any one of claims 1 to 18 or to a fusion protein according to claim 19 or claim 20.

22. A nucleic acid molecule encoding a tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1-18 or a fusion protein according to claim 19 or 20.

23. An antisense nucleic acid molecule which binds under high stringency conditions to a nucleic acid molecule according to claim 22.

24. A vector comprising a nucleic acid molecule according to claim 22 or claim 23.

25. A host cell transformed or transfected with a nucleic acid molecule according to claim 23 or a vector according to claim 24.

26. A method for preparing a tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1 to 18 or a fusion protein according to claim 19 or 20 comprising culturing a host cell containing a nucleic acid molecule according to claim 22 under conditions whereby said protein is expressed and recovering said protein thus produced.

27. A method of identifying an activator compound that inhibits autoinhibition of c-Abl by the cap region comprising contacting c-Abl with a candidate activator compound and assessing whether binding between the cap region of c-Abl and the catalytic and SH2 and/or SH3 domains of c-Abl has been inhibited.

28. An activator compound identified or identifiable by the method of claim 27.

29. A method for identifying a modulator compound that restores autoinhibition of c-Abl by the cap region comprising contacting c-Abl and an activator compound according to

claim 28 with a candidate modulator compound and assessing whether binding between the cap region of c-Abl and the catalytic and SH2 and/or SH3 domains of c-Abl is restored.

30. A modulator compound identified or identifiable by the method of claim 29.

31. A method of modulating the activity of a protein tyrosine kinase comprising providing a cell with a tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28 or a modulator compound according to claim 30.

32. Use of a cap region of a c-Abl protein or a functional equivalent thereof as a tyrosine kinase inhibitor.

33. A tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28 or a modulator compound according to claim 30 for use as a pharmaceutical.

34. A pharmaceutical composition comprising a tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28 or a modulator compound according to claim 30 in conjunction with a pharmaceutically-acceptable carrier molecule.

35. Use of a tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28, a modulator compound according to claim 30, or a pharmaceutical composition according to claim 34 in the manufacture of a medicament for the treatment of a disease assciated with aberrant tyrosine kinase activity.

36. A method of treating a disease associated with aberrant tyrosine kinase activity in a patient, comprising administering to the patient a tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1-18, a fusion protein

according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28, a modulator compound according to claim 30, or a pharmaceutical composition according to claim 34.

37. Use according to claim 35 or method according to claim 36 wherein said disease is a neurological disease or cancer.

38. Use or method according to claim 37 wherein said disease is leukaemia.

39. A method of diagnosing a condition associated with an aberrant activity of a tyrosine kinase protein comprising measuring the level of an aberrant tyrosine kinase protein in a cell sample obtained from a patient using a tyrosine kinase inhibitor protein according to any one of claims 1-18.

40. A method of diagnosing a condition associated with an aberrant tyrosine kinase activity of c-Abl protein comprising using a nucleic acid molecule according to claim 22 or an antisense nucleic acid molecule according to claim 23 to screen for mutations in the cap region.

41. A transgenic animal comprising a nucleic acid molecule according to claim 22.

42. A c-Abl protein comprising a protease cleavage site located near the boundary of the cap region and the SH3 domain.

43. A c-Abl protein according to claim 42 wherein said protease cleavage site is a TEV protease cleavage site.

44. A fusion protein comprising a c-Abl protein according to claim 42 or claim 43 fused to a marker domain.

45. A method for activating the tyrosine kinase activity of c-Abl comprising supplying a cell with a c-Abl protein comprising a protease cleavage site according to claim 42 or claim 43 or a fusion protein according to claim 44 and supplying the cell with a protease to cleave at the protease cleavage site.

46. A method for producing an activated c-Abl protein comprising cleaving a c-Abl protein according to claim 42 or claim 43 or a fusion protein according to claim 44 with a protease and isolating the cleaved C-terminal region of said c-Abl protein.

47. A method for producing a tyrosine kinase inhibitor protein comprising cleaving a c-Abl protein according to claim 42 or 43 or a fusion protein according to claim 44 with a protease and isolating the cleaved N–terminal cap region of said c-Abl protein.

48. A nucleic acid molecule encoding a c-Abl protein according to claim 42 or claim 43 or a fusion protein according to claim 44.

49. A method for activating a c-Abl protein comprising introducing a nucleic acid molecule according to claim 48 into a cell under conditions in which it is expressed and supplying said cell with a protease.

50. A method for producing an activated c-Abl protein comprising inroducing a nucleic acid molecule according to claim 48 into a cell under conditions in which it is expressed, supplying said cell with a protease and isolating the cleaved C-terminal region of said c-Abl protein

51. A method for producing a tyrosine kinase inhibitor protein comprising introducing a nucleic acid molecule according to claim 48 into a cell under conditions in which it is expressed, supplying said cell with a protease and isolating the cleaved N-terminal cap region of said c-Abl protein.

52. A transgenic animal comprising a nucleic acid molecule according to claim 48.

53. A method for activating tyrosine kinase activity of c-Abl *in vivo* comprising supplying a transgenic animal according to claim 52 with a protease.

54. A method for screening for a compound that restores autoinihibition of c-Abl *in vivo* comprising supplying a transgenic animal according to claim 52 with a protease to activate the tyrosine kinase activity of c-Abl, supplying the transgenic animal with a candidate compound and assessing the effect of the candidate compound on the tyrosine kinase activity in the cells of said transgenic animal.